Translation

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Form PCT/IPEA/416
16058/PCT ps		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP2004/004984	10.05.2004	09.05.2003
International Patent Classification (IPC) or national classification and IPC		
Applicant		
EVOTEC TECHNOLOGIES GMBH		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 8 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *(sent to the applicant and to the International Bureau)* a total of 5 sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s))

      _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
Name and mailing address of the IPEA/EP Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2004/004984

Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language _____, which is the language of a translation furnished for the purposes of:

☐ international search (Rule 12.3 and 23.1(b))

☐ publication of the international application (Rule 12.4)

☐ international preliminary examination (Rule 55.2 and/or 55.3)

2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☐ the international application as originally filed/furnished

☒ the description:

pages 1-23 as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☒ the claims:

nos. _____ as originally filed/furnished

nos.* _____ as amended (together with any statement) under Article 19

nos.* 1-25 received by this Authority on 12.01.2005 with letter of 12.01.2005

nos.* _____ received by this Authority on _____

☒ the drawings:

sheets 1/12-12/12 as originally filed/furnished

sheets* _____ received by this Authority on _____

sheets* _____ received by this Authority on _____

☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____

☐ the claims, nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2004/004984

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-25	YES
	Claims		NO
Inventive step (IS)	Claims	8, 10-12	YES
	Claims	1-7, 9, 13-25	NO
Industrial applicability (IA)	Claims	1-25	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

1 This report makes reference to the following documents:

D1: US 6 400 453 B1 (HANSEN W PETER) 4 June 2002 (2002-06-04)

D2: US 5 138 181 A (CHAMPSEIX HENRI ET AL) 11 August 1992 (1992-08-11)

D3: US 2003/040105 A1 (GALLEGOS CARLOS M ET AL) 27 February 2003 (2003-02-27)

D4: WO 02/065121 A (KEHLENBECK MARKUS; ROTHAUSZKY DAGMAR (DE); EVOTEC AG (DE); PUMP DENNI) 22 August 2002 (2002-08-22)

D5: US 5 542 305 A (HOLLINGER JOHN D) 6 August 1996 (1996-08-06)

2 INDEPENDENT CLAIM 1

2.1 The present application does not meet the requirements of PCT Article 33(1) because the subject matter of the amended claim 1 does not involve an inventive step within the meaning of PCT Article 33(3).

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

2.2 D3, which is considered to represent the closest prior art, describes a micromixing device which, in the embodiments shown in figures 7 and 8, is explicitly free of dead volume spaces (D3, paragraphs [0110] and [0111]) and is also suitable as embodied for mixing particles using a carrier flow and which anticipates all the technical features of the original claim 1 (see the passages referred to in the search report). The features of the amended claim 1 anticipated by D3 form the preamble of this claim. The amended claim additionally contains the technical features of the original dependent claim 8, which now form the characterizing part of claim 1: that is, that the particle injector is "characterized in that the injection channel (...) has a cross section which tapers towards the carrier channel".

2.3 The purpose of this feature is (1) to facilitate the introduction of a dispensing device, for example, an injection needle, into the carrier flow channel without fracturing and (2) to reduce sedimentation by the particles in the injection channel by an increased flow rate towards the carrier channel.

2.4 Both the technical problems mentioned in 2.3 above and the solution thereof, namely, that the injection channel tapers towards the carrier channel, represent common general knowledge among specialists in the field of flow cytometry using microfluidic systems and therefore cannot

substantiate inventive step with respect to claim 1. Moreover, a person skilled in the art wishing to solve the problem of feeding a sample into the injection channel in a reliable and fracture-free manner using a dispensing device, such as an injection needle, generally having a conically tapering tip, would, in addition to the literature relating to microfluidic system injectors, also consider injectors in related technical fields, such as classic flow cytometry, since (a) these fields address precisely the same problems as those described above in 2.3, (b) the materials in which the channels are installed (for example, glass) are not invariably different from those of microfluidic systems having a similar function ("cell sorters") and (c) processes for producing miniaturized flow cytometers, that is, specialized microfluidic systems, are common general knowledge in the art and therefore the features, suitably adapted, that is, appropriately reduced in size, known from classic flow cytometers can be transferred to microfluidic flow cytometers.

However, the literature of classic flow cytometry reveals numerous documents describing injectors having injection channels which taper towards the carrier channel. D2, which is cited merely as an example, describes a flow cytometer which can be used for counting and determining leukocyte subpopulations using the injection device 16, which serves to feed leukocyte solutions via a conically tapering channel 20 (D2, column 4, lines

21-25 and 36-38, and figure 1). D2 also describes a further, external injector 10 for the carrier fluid, said external injector in turn receiving the inner injector, that is, the dispensing device for the sample solution, and likewise tapering conically towards the carrier channel (column 4, lines 9-25). Therefore, neither the technical problems shown in 2.3 nor their solution can be considered to involve an inventive step and claim 1 consequently does not meet the requirements of PCT Article 33(1) and (3).

3. D3 relates (embodiments in figures 7 and 8) (see D3, paragraphs [0110] and [0111]) to a microfluidic system (D3, paragraphs [0006]-[0009]). Consequently, the additional technical features of claim 20 are known from D3, where they are used for the same purpose. Therefore, claim 20 fails to meet the requirements of PCT Article 33(1) and (2).

4. Further, dependent claims 2-4, 7 and 13, 14 and 16-25 also do not meet the requirements of PCT Article 33(1) and (3), since all their technical features are known, explicitly or implicitly, from D1, D3, D4 and D5.

D1, D4 and D3 describe:

D1: a classic flow cytometer with reduced dead volume spaces for centring and orienting microorganisms (column 8, line 48 to column 9, line 30 and figures 1 and 2);

D4: a dispensing device for dispensing small volumes of a liquid cell suspension, said device being likewise suitable for mixing a particle (cell) suspension with a solution, for example, a carrier fluid, from a second reservoir, wherein the contact element between the feeds and the outlet is free of dead volume spaces (page 10, paragraph 2);

D5: an inlet valve free of dead volume spaces for a flow cytometer with a sample stream and a sheath flow (column 2, lines 56-65).

5. Further, the application does not meet the requirements of PCT Article 33(1) and (3) because the subject matter of dependent claims 5, 6, 9 and 15 does not involve an inventive step within the meaning of PCT Article 33(3):

The technical features of claims 5, 6 and 9 used for the same or similar technical purposes are known from the combination of D1 and D2 (see the passages referred to in the search report). D2 describes a particle injector for counting leukocytes, said particle injector having a centring device for the injection nozzle and a screw-off end piece on the dispensing line.

The technical features of claim 15 used for the same or similar technical purposes are known from D4 (wherein, in D4, only part of the injector can be autoclaved).

Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

6. The technical features of claims 8 and 10-12 do not appear to have been anticipated by any of the prior art documents.